Non-technical abstract

Treatment is a critical problem in the management of severe Peripheral Artery Occlusive Disease (PAOD). Three therapeutic approaches are usually considered for patients suffering from PAOD (Isner & Rosenfield, 1993):

1) risk factor modification, such as tobacco, dietary changes, etc.;
2) when possible, percutaneous transluminal angioplasty (PTA) to revascularize the ischemic limb;
3) bypass surgery with the use of prosthetic material or vein graft. Both PTA and especially surgery carry a significant morbidity/mortality in these patients who often suffer concomitantly from an already existing heart or disseminated vascular disease.

Therapeutic angiogenesis is a recent concept based on the use of factors with the potential to stimulate development of new blood vessels for the treatment of tissue ischemia such as that observed in limb or heart muscle due to severe atherosclerosis. Both the administration of angiogenic factors in the form of a recombinant protein, or as a gene therapy has been shown to induce angiogenesis in a number of animal models, as well as very recently in humans. Baumgartner et al. (1998) published results of a clinical trial evaluating the angiogenic factor Vascular Endothelial Growth Factor (VEGF) delivered as a gene therapy in patients with severe limb ischemia. This study established the proof of concept for therapeutic angiogenesis indicating that VEGF gene therapy using a non viral DNA plasmid was sufficient to induce clinical activity in patients with severe limb ischemia.